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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,532	08/24/2001	Michael Damm	0691-072	2488

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EXAMINER
GUPTA, ANISH

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,532	DAMM ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 08/17/00 . It is noted, however, that applicant has not filed a certified copy of the German priority application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

2. The information disclosure statement filed 06-25-02 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. The explanation provided by Applicant in the submission does not constitute a "concise explanation." It has been placed in the application file, but the information referred to therein has not been considered.

Particularly, the references WO 99/36099, lottspeich et al. and Neumuller et al. have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the claim recites "free basic peptide" or a "basic starting peptide". It is unclear what is defined to be a free basic peptide. It is unclear how the peptide is "free" and from what it is "free." It is unclear if the "basis" makes reference to pH or is used in some other connotation.

In claim 1, the claim states that the method "comprises reacting an acid addition salt of a basic starting peptide in the presence of a diluent in a mixed bed ion exchanger." However, the claim also states, with respect to the desired product, "forming the desired acid addition salt of the peptide, and removing the diluent." It is unclear as to the starting material peptide. The claim implies that the starting peptide is a "acid addition salt" and the desired product is also an "acid addition salt." Are the starting material and the end products the same or different? If the acid salts are different, then the claim should indicate how the peptide salts, as the starting material, differ from the peptide salts as the final product.

Claim 1 is very unclear. Applicants are requested to amend the claim to specifically indicate what are the method step in the method for producing peptide salts. For example, it is unclear as the relationship of "mixture of an acid and a basic ion exchanger during the formation of a free basic peptide" to the other steps. Some clarification for the method steps is requested for this claim.

In claim 1, in the sentence "mixture of an acid and a basic ion exchanger during the formation . . . ," it is unclear if there is the presence of an acid and a basic ion exchanger or if there is a mixture of an acid ion exchanger or basic ion exchanger.

In claim 1, there seems to be a method step missing since after the isolation of the "free basic peptide," it is unclear how the acid addition salts are formed.

In claim 2, there is grammatical error since the word starting is misspelled.

In claim 3 and 4, the claims list acids. However, it is unclear which acids these are in claim 1. That is, are these acids the inorganic or organic acids or the acid mixed during the formation of a free basic peptide.

In claim 5, there is grammatical error since the word diluent is misspelled.

Claim 9 is indefinite since it is unclear for what treatment the peptide salt is to be used. It is unclear what treatments are intended to be part of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Engel et al.

4. The claims are drawn to a pharmaceutical formulation of a peptide and a carrier and method of using said peptide composition.

The reference teaches a pharmaceutical formulation of the LHRH analog Cetrorelix in the form of a ebmonic acid salt and Cetrorelix acetate (see col. 5, lines 5-25 and claims). The reference states that both of these peptides are effective in the suppressing LH and FSH and tumor growth (see col. 1, lines 21-30 and col. 4, lines 8-14). Although the reference does not teach the method of

making, the instant claims are a product by process claims. The MPEP states "'even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.'" MPEP 2113. Thus, since the reference teaches a peptide salt and a method of treatment using the peptide salt, the limitation of the product has been met and therefore the determination of the patentability has been made.

5. Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Schally et al.

The claims are drawn to a method of making peptide salts.

Schally et al. teach the conversion of LHRH antagonists from a hydrogen fluoride salt to acetic acid salt by subjecting the dissolved hydrogen fluoride salt peptide to a cation exchange column that has been equilibrated with acetic acid and washed with deionized water (see col. 13, lines 6-15). The procedure yields an acetic acid salt product of the LHRH antagonist after lyophilization (see col. 13, lines 15-16). The method disclosed reads on claimed invention since the reference discloses the use of a resin to convert one acid salt to another acid salt. The reference also discloses the use of organic acid, acetic acid, to displace the fluoride salt to attain an acetic acid salt..

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coy et al. and Schally et al. in view of Engle et al.

The claims are drawn to a method of making a peptide salt of Cetrorelix.

6. Coy et al. teach that peptides such as LHRH analogs can be obtained in form of a acid salt and "[i]f desired, a particular acid addition salt is converted into another acid addition salt, e.g. a salt with a non-toxic, therapeutically acceptable acid, by the treatment with appropriate ion exchange resin." The reference teaches that both cation exchanger and anion exchanger will accomplish this task (see col. 4, lines 39-62). Schally et al. reflects this process since it teaches the conversion of LHRH antagonists from a hydrogen fluoride salt to acetic acid salt by subjecting the dissolved hydrogen fluoride salt peptide to a cation exchange column that has been equilibrated with acetic acid and washed with deionized water (see col. 13, lines 6-15). The procedure yields an acetic acid

salt product of the LHRH antagonist. The reference also discloses the peptide Cetrorelix as one of its LHRH antagonist, where the sequence is Ac-DNal-DpCl-Phe-DPal-Ser-Tyr-DCit-Leu-Arg-pro-D-Ala-NH2 (see claim 1). The difference between the prior art and the instant application is that the reference does not teach the a embonic acid salt product of Cetrorelix.

However, Engle et al. teach that for LHRH antagonist, Cetrorelix acetic acetate, obtained in Schally et al., the duration of action could not be extended once a threshold dose was reached (see col. 2, lines 1-14). Engle et al. taught that embonic acid salts of Cetrorelix would have an unexpected prolongation of action and improved effect without using biologically degradable polymers and fats (see col. 4, lines 7-14 and abstract). The method disclosed to make the Cetrorelix embonate by dissolving Cetrorelix acetate and embonic acid in a molar ratio of 2:1 of peptide: embonic acid. This results in a white precipitate and this is filtered and dried. The dried precipitate is moistened with ethanol and vacuum dried (lyophilized) (see examples 2 and 4 in col. 5-6). Therefore it would have been obvious to subject the Cetrorelix acetate obtained in Schally et al. to the procedure in Engle to obtain the desired Cetrorelix embonate salt. One would be motivated to this since the Cetrorelix embonate salt would have an unexpected prolongation of action and improved effect without using biologically degradable polymers and fats. The procedure of combining the teachings of Schally and Engle would read on the claimed method. For example, Schelly teaches the reaction of the starting peptide salt with the resin, while Engle teaches the formation of the desired acid salt.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to

reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

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